

REMARKS/ARGUMENTS

Claims 1-4 and 7-23 were pending at the time of the mailing of the final Office Action. A Response after Final Office Action was submitted on 7 December 2009. An Advisory Action was issued on 17 December 2009, refusing entry of the amendment on the ground that the amendment raised new issues that would further consideration and/or search. By this amendment, claims 1-3 and 19-23 are cancelled without prejudice or disclaimer of the subject matter contained therein. Claims 4, 9-13 and 15-18 have been amended. Claims 8, 10, 11 and 16-18 were previously withdrawn from consideration.

In the Office Action of 5 October 2009, claims 4, 7, 9, 12, 13 and 15 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failure to point out and distinctly claim the subject matter of the invention. Claims 4 and 7 were rejected as unpatentable under 35 U.S.C. § 103(a) over U.S. Pat. Pub. No. US2002/004060 to Heublein et al. (hereinafter “Heublein”). Claims 9 and 15 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Heublein as applied to claims 4 and 7 and in further view of The Columbia Electronic Encyclopedia, 6th Edition, 2007. Claims 9 and 12-15 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Heublein as applied to claims 4 and 7 and in further view of GB 1378281 to Tikova et al (hereinafter “Tikova”) and ASM International Metals Handbook, Vol. 2, 1997 (hereinafter “ASM”).

Claims 4, 9-13 and 15-18 have been amended to recite language consistent with the previous amendment of claim 4, which replaced a recitation of “a pharmaceutical formulation” with a recitation of “an endoprosthesis.” Therefore, proper antecedent basis is believed to be provided for all the elements of claims 4, 9-13 and 15-18. Withdrawal of the rejection under 35 U.S.C. § 112, second paragraph is respectfully requested.

Claims 4 and 7 stand rejected as obvious over Heublein. To establish obviousness, there must be some teaching, suggestion, or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. (MPEP § 2143). Additionally, the references must be must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination. (MPEP § 2141). There must also be a reasonable expectation of success. (MPEP § 2143.) The Applicants respectfully maintain that Heublein, considered as a whole, does not suggest the desirability of the present invention.

In response to the Applicants' previous arguments, it was alleged that the present invention was obvious over Heublein in part because "examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments." However, Applicants' prior remarks concerning Heublein were not intended to indicate that Heublein teaches away from the present invention, but rather that Heublein's disclosure is so expansive that it can not constitute a teaching or suggestion of the present invention, much less provide a reasonable expectation of success. By way of example, a disclosure of the periodic table of elements would obviously be so broad as to not suggest or predict any particular invention, while the specific disclosure of one element clearly would suggest the same invention. As a disclosure becomes broader and includes more possibilities, at some point the disclosure becomes so broad and the components taught are so varied that the invention in question would not be reasonably predictable to one of ordinary skill in the art. The Applicants maintain that this is the case with the teaching of Heublein. When Heublein is considered as a whole, the modification alleged by the Examiner is not suggested by Heublein but can only be the result of impermissible hindsight.

As stated previously, the compositions disclosed in Heublein include a wide variety of potential components but Heublein provides no actual guidance as to advantages or disadvantages of any of them as they relate to the present invention. For example, Heublein provides as potential components of the stent “pure iron,” alloys or sintered metals having a main constituent selected from the group of alkali metals, of alkaline earth metals, iron, zinc or aluminium. (paragraph 0013). At least 23 possible “subsidiary constituents” of the alloy are also indicated (paragraph 0014). “Other metals and rare earths” are also disclosed as potential components (paragraph 0016). Furthermore, Heublein clearly indicates that a magnesium alloy containing up to 40 % lithium is preferred (paragraph 0014). Clearly, one of ordinary skill in the art would not consider such a diverse group of alloys to all inhibit smooth muscle cell proliferation in the absence of a clear teaching of such an effect. The alleged obviousness can not be said to arise from a choice from a finite number of identified, predictable solutions with a reasonable expectation of success.

In the Advisory Action of December 17, 2009, it was indicated, “Heublein specifically teaches magnesium with one of six preferred compositions, three of which contain rare earths, particularly neodymium as a choice of 4 rare earths (see paragraphs 16-21) and therefore, one skilled in the art reasonable guidance to select magnesium with neodymium.” As stated previously, the disclosure of Heublein should be considered as a whole and individual paragraphs should not be interpreted in isolation. However, even if these paragraphs are considered separately, they do not provide the specific guidance indicated. For example, paragraphs 15 and 16 provide a magnesium alloy that may contain up to 40 percent lithium, or no lithium at all. The same composition may or may not contain iron. The same composition contains “less than 5% other metals or rare earths.” The absence of rare earths is equally taught by this passage as the

presence of rare earths. Furthermore, Heublein teaches here that rare earths are as equally desirable as “other metals.” Such a disclosure, which provides that lithium, iron and rare earth elements may or may not be present, can not be considered enabling of any particular formulation, much less the formulation claimed. Nor is intravascular liberation of yttrium, neodymium or zirconium or the inhibition of smooth muscle cell proliferation taught or suggested.

Likewise, paragraph 17 also provides that lithium may or may not be present. While neodymium is mentioned, it is only mentioned as one of 4 possible rare earth elements. No teaching or suggestion is made of intravascular liberation of neodymium or the inhibition of smooth muscle cell proliferation.

As with paragraph 16, paragraph 19 teaches that lithium may or may not be present and paragraph 21 teaches that “other metals and/or rare earths” may or may not be present. As with paragraph 16, these paragraphs can not be considered enabling of any particular formulation, much less the formulation claimed. A teaching or suggestion of intravascular liberation of yttrium, neodymium or zirconium or the inhibition of smooth muscle cell proliferation is also absent from these paragraphs.

In the Advisory Action, it was also indicated that Heublein provides zirconium as “one about 20 choices for the subsidiary constituent with magnesium or iron (paragraphs 13 and 14).” This was cited as supporting the position that the selection of zirconium with magnesium or iron would have been within the purview of one of ordinary skill in the art. However, the entirety of this disclosure of Heublein should also be considered. Among the 23 possible subsidiary components provided by Heublein, in addition to zirconium, are lead and thorium. One of skill in the art would have recognized such components as being undesired in an implantable medical

device. Lead would have been disfavored as a heavy metal. The toxic effects of ingestion of lead are well known. Thorium is a radioactive metal that would also have been disfavored by one of ordinary skill in the art. Therefore, this disclosure of Heublein is so expansive as to include metals which would clearly be disfavored for use in an implantable medical device, such as an endoprosthesis. For this reason, a person having ordinary skill in the art would have questioned the value of this teaching of Heublein and would not have relied upon Heublein regarding possible components of an endoprosthesis. Heublein can not be considered enabling of the present invention.

Therefore, it can not be said that the claims would have resulted from combining known elements to yield predictable results, or that they would have resulted from simple substitution of one known element for another to obtain predictable results. Furthermore, the invention did not involve use of a known technique to improve a similar device in the same way. Nor did the modification in question involve the applying of a known technique to a device, method or product ready for improvement to yield predictable results. No allegation was made that known work in one field or a different one would prompt variations of it for use in the same field or a different one, based on design incentives or other market forces, to provide predictable results. Therefore, one of ordinary skill in the art would not find any suggestion or motivation, either in Heublein or in the knowledge generally available to one of ordinary skill in the art, to modify Heublein to arrive at the invention recited in claims 4 and 7. For this reason, these claims patentably distinguish over Heublein. Withdrawal of the rejection of claims 4 and 7 under 35 U.S.C. § 103(a) is again respectfully requested.

Claims 9 and 15 stand rejected as being obvious over Heublein as applied to claims 4 and 7 and in further view of The Columbia Electronic Encyclopedia, 6th Edition, 2007. The remarks

made above regarding the distinctions between Heublein and claims 4 and 7 are repeated herein with regard to claims 9 and 15. In response to the Applicants' previous comments, the Examiner maintains that one of skill in the art would have been motivated "to manipulate the amount of yttrium by routine experimentation to optimize the properties of the resultant formulation including efficacy, stability and rate of degradation." However, given the expansive disclosure of Heublein, discussed above, the amount of experimentation required to do this could not be considered "routine." As discussed previously, rare earth elements are only generally disclosed by Heublein as one of many potential components and among these, yttrium is not specifically disclosed, although other rare earth elements are disclosed. As also stated previously, neither reference provides a teaching or suggestion of delivery of yttrium to the smooth muscle cells in the range of 200 μ M and 2 mM as recited in claim 15. In fact, neither of the cited references provides one of ordinary skill in the art with any guidance on the desirability of delivery of yttrium at all, much less at the specified concentrations. Therefore, one of ordinary skill in the art would have had no reasonable expectation of success in combining the teachings of the cited references. Claims 9 and 15 patentably distinguish over Heublein in view of The Columbia Electronic Encyclopedia. Withdrawal of the rejection of claims 9 and 15 under 35 U.S.C. § 103(a) is respectfully requested.

Claims 9 and 12-15 stand rejected as being obvious over Heublein as applied to claims 4 and 7, and further in view of Tikhova and ASM. In the final Office Action, it was maintained that Tikhova teaches that yttrium and neodymium provide high creep resistance and improved thermal stability, and that zirconium provides a fine-grained structure. However, even assuming that Tikhova does provide such properties, it only does so in the context of light structural alloys, particularly those for the production of parts subject to heating in service (column 1, lines 17-20).

Table 1 of Tikhova provides for properties of these alloys at room temperature, 300°C and 400°C, for example. Clearly, Tikhova does not contemplate the use of such alloys in the medical field, much less as an endoprosthesis. Tikhova makes no suggestion that the alloy disclosed is biocompatible or has any properties that would be necessary for its suitability in an endoprosthesis.

ASM was indicated to teach that WE43 is a known Mg-Y-Nd-Zr alloy. However, no teaching of the WE43 alloy is observed in ASM, although another alloy, WE54, was taught. Additionally, as with Tikhova, ASM provides alloys intended for vastly different applications than endoprostheses, addressing properties such as strength at temperatures as high as 600 °F and corrosion resistance under salt fog conditions (see Abstract). No teaching or suggestion is made in ASM that the alloy disclosed is biocompatible or has any properties that would be necessary for its suitability in an endoprosthesis. Therefore, one of ordinary skill in the art would not rely on either Tikhova or ASM for a predictable result regarding the use of the disclosed alloys in an endoprosthesis with a reasonable expectation of success.

Furthermore, the remarks made above regarding the distinctions between Heublein and claims 4 and 7 are repeated herein with regard to claims 9 and 12-15. Therefore, claims 9 and 12-15 patentably distinguish over Heublein in view of Tikhova and ASM. Withdrawal of this rejection of claims 9 and 12-15 under 35 U.S.C. § 103(a) is respectfully requested.

Because the amendments presented herein place the claims under consideration in condition for allowance, entry of this Amendment after Final Rejection is appropriate. Furthermore, because claim 4 is believed to be generic for all species within elected Invention II, rejoinder of non-elected claims 8, 10-11, and 16-18 is hereby requested. Amendments to claims 4, 9-13 and 15-18 address the rejection under 35 U.S.C. § 112, second paragraph. None of the

amendments will necessitate an additional search. In the event that the Examiner disagrees with the Applicants regarding the allowability of the pending claims, entry of the Amendment should still be made on the grounds that the amendments of claims 4, 9-13 and 15-18 and cancellation of claims 1-3 and 19-23 simplifies matters under consideration for appeal.

The outstanding Office Action was electronically transmitted on 5 October 2009. The Examiner set a shortened statutory period for reply of 3 months from the mailing date. Therefore, no petition for an extension of time in making this response is believed to be due. However, the Applicants hereby make a conditional petition for any extension of time for response in the event that such a petition is required. The Commissioner is authorized to charge any fee required with this paper or to credit any overpayment to Deposit Account 15-0450.

Respectfully submitted,

/John J. Cunniff/

John J. Cunniff
Reg. No 42,451
Attorney for Applicants

Hahn Loeser + Parks LLP
One GOJO Plaza
Suite 300
Akron, OH 44311